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REDUCTIVE TRANSFORMATIONS WITH TRIMETHYLSILYL CHLORIDE-SODIUM IODIDE. A NEW SYNTHESIS OF 4H-1,3-OXAZINES[1].

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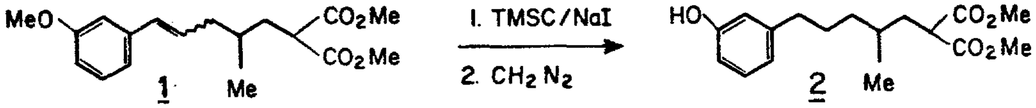
Abstract: 1-Arylalkenes and 1-arylalkanols are reduced to arylalkanes on heating with trimethylsilyl chloride/sodium iodide in CH_3CN. Under similar conditions enones, dialkylated in the β-position of the double bond, give 4H-1,3-oxazines.

The versatility of iodotrimethylsilane as a useful reagent in organic synthesis is well established[2]. The reductive properties of this reagent, prepared in situ from trimethylsilyl chloride (TMSC) and sodium iodide, have been evidenced in the reduction of double bonds of β-phenyl-α,β-unsaturated carbonyl compounds[3a] and enediones[3b], deoxygenation of α-hydroxyketones[4] and dehalogenation of α-halogenoketones[5]. We report herewith on the extension of these properties, namely, the reduction of 1-arylalkenes and the reductive dehydroxylation of secondary and tertiary benzylic hydroxyl groups. We also describe a new TMSC/NaI-mediated annulation of some α,β-unsaturated ketones, with the participation of the solvent (CH_3CN), to form 4H-1,3-oxazines.

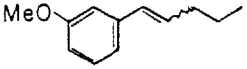
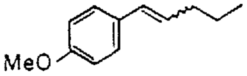
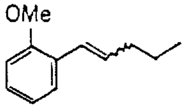
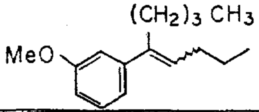
While attempting to cleave the aryl methoxy group in 1, an intermediate for a natural product synthesis, we found that under standard dealkylation conditions (TMSC-NaI, reflux)[6], followed by esterification of the resulting diacid, the saturated phenolic derivative 2 (71%) was obtained[7]. This reduction of a double bond conjugated with an aryl group was found to be general and can be effected with some selectivity in the presence of methoxy substituents in the aromatic ring (Table I).



In a typical experiment, a mixture containing the alkene (1 mmol), benzoic acid (1 mmol) TMSC (3 mmol), NaI (3 mmol) and CH_3CN (2 ml) was stirred in a 10 ml flask under argon for 30 min., then heated to 75°C for the indicated time. The dark brown solution was diluted with ether, washed successively with aqueous $Na_2S_2O_3$, $NaHCO_3$ and brine, dried ($MgSO_4$) and purified by chromatography. We were able to show that the reductive process consists of two steps: (a) hydroiodination at room temperature[8] and (b) and reductive dehalogenation of the benzylic iodo-derivative, on heating. The latter step may be explained by hydride transfer from trimethylsilane[9], generated according to the equilibrium:

$$Me_3SiI + HI \rightleftharpoons Me_3SiH + I_2$$

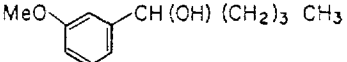
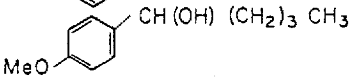
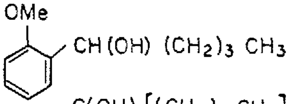
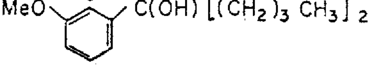
TABLE 1

Entry	Alkene	Time(h)	Yield[a] alkane(%)	methoxy:phenol ratio
1	$PhCH=CH(CH_2)_4CH_3$	20	71[b]	
2	INDENE	16	98[c]	
3		7	74	77:23
4		7	90	78:22
5		7	76	74:26
6		7	87	94:6

[a] Methoxy and hydroxyalkanes (entries 3-6) were chromatographically isolated; [b] ~15% of alkene was recovered; in entries 3-6 the recovery was 5-10%; [c] indane.

Utilization in the above reactions of 3 mmol of benzoic acid, to convert fully Me_3SiI into HI, resulted in inferior yields, with more alkene recovered and therefore the assumption that HI is solely responsible for the dehalogenation, as presumed for electrophilic β-phenyl alkenes[3d], is less probable. Addition of AIBN to the reaction mixture also provided inferior results and therefore hydrogen donation by a radical mechanism seems improbable.

TABLE II

Alcohol	Time(h)	Yield[a] alkane(%)	methoxy:phenol ratio
$PhCH(OH)(CH_2)_3CH_3$	20	75	
	7	85	78:21
	7	85	71:29
	7	84	77:23
	7	94	72:28

[a] About 5-8% of the corresponding alkenes (not included in the yield) were also obtained

We found that reductive dehydroxylation *of secondary or* tertiary benzylic alcohols, (via the iododerivatives[6]) can similarly be achieved by means of TMSC/NaI (Table II)[10]. Previous dehydroxylations by hydrogen-devoid silanes, (diiodimethylsilane/NaI[11] and dichlorodimethylsilane/NaI[12] were limited to tertiary benzylic alcohols and carbinols with more than one vicinal aryl group.

Exposure of α,β unsaturated ketones to TMSC/NaI affords β-iodoketones[13]. We found that enones 3, *possessing two alkyl substitents at* the β position of the double bond, are smoothly converted under our conditions[10] to 4H-1,3-oxazines 5 (Table III). Hence acetonitrile participates in the reaction by attack on the tertiary carbocation which is formed via the assumed intermediate 4. Absence of inverse electron demand

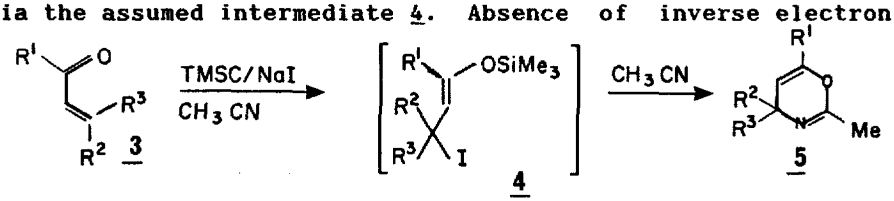
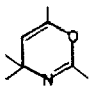
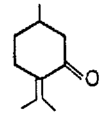
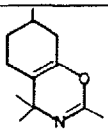
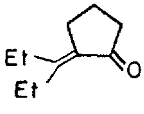
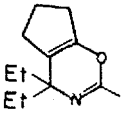
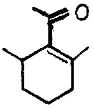
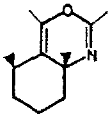
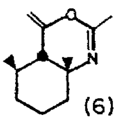


TABLE III

Enone	Time (h)	Product[a]	Yield(%)
Me$_2$C = CHCOMe (3a)	7	 (5a)	70
 (3b)	7	 (5b)	89
 (3c)	4.5	 (5c)	62
 (3d)	4.5	 (5d)  (6)	71

[a] The products were identified by ¹HNMR[17], ^{13}C NMR and MS. [b] The ratio 1:5 for 5d:6 was approximated by help of ^{13}C NMR spectrum of the mixture and the stereochemistry was assigned by ¹H and ^{13}C NMR spectral analysis.

makes improbable a hetero-Diels-Alder reaction[14]. Indeed, in the absence of TMSC/NaI, Lewis acid catalysis ($BF_3.Et_2O$) in refluxing CH_3CN did not convert 3b into 5b. Formation of the double bond regioisomer 6 as the major product from 3d is attributed to the steric hindrance produced by the 1,3 methyl-methyl interaction in 5d.

A mechanistically similar previous synthesis of 1,3-oxazines from β-chloroketones and nitriles, promoted by $SnCl_4$, presented limitations: successful results were obtained solely by the utilization of aryl ketones and aromatic nitriles[15] whereas other nitriles led to a mixture of oxazines (25-40%) and open-chain β-ketoallylamines.[16] To the best of our knowledge, the new entry into 4H-1,3-oxazines represents the first example of a formal 4+2 type cycloaddition of an enone to a nitrile and an unprecedented participation of the solvent in TMSI-mediated reactions.

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17. ^{1}HNMR ($CDCl_3$) 5a, δ 1.16(6H,S), 1.75(3H,s), 1.94(3H,S), 4.59(1H,s); 5b, δ 1.0(3H,dJ=6Hz), 1.22(6H,s), 1.19-1.23(1H,m), 1.64-1.85(3H,m), 1.92(3H,s), 2.0-2.10(3H,m); 5c, δ 1.73(6H,t), 1.39-1.54(4H,m), 1.78-1.91(2H,m), 2.01(3H,s), 2.11-2.48(m,4H); 5d, (CH_3 groups) δ 1.13(3H,d,J=6H_z), 1.23(3H,s), 1.78(3H,s), 1.93(3H,s); 6, δ 0.9-1.88(8H,m), 0.91(3H,s), 1.05(3H,s), 1.98(3H,s), 4.09(1H,s), 4.59(1H,s).

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